REMARKS

Preliminary Remarks

Reconsideration and allowance of the present application based on the following remarks are respectfully requested. Claims 16-23 are currently pending and remain at issue in this application.

The applicants do not intend by these or any amendments to abandon the subject matte of the claims as originally filed or later presented, and reserve the right to pursue such subject matter in continuing applications.

Petition

The applicants hereby request a petition for an extension of time to file this response in the third month. Per the enclosed RCE form, the USPTO is authorized to charge the associated fees to the undersigned's firm's deposit account.

RCE

By the enclosure, the applicants have requested entry of this amendment and response and have further requested removal of the finality of the outstanding official action.

Additional Fee

Although the applicants believe additional fees (beyond those presented herein) are not necessary for entry and consideration of this amendment/response, should the USPTO determine additional fees are due (for such consideration), the Patent Office is authorized to charge such fees to USPTO Deposit Account No. 03-3975.

Patentability Remarks

Rejection Pursuant to 35 U.S.C. §112, Second Paragraph

In paragraphs 2-6 of the official action, the examiner rejected claims 18, 21, and 23 for allegedly being indefinite. Specifically, the examiner alleged that claims 18 and 21 were indefinite because it lacked proper antecedent basis for the vector. With regard to claim 22, the examiner alleged that the recitation of a "gene encoding for S-(2-aminoethyl)-cysteine resistance" was unclear as to how a gene can encode resistance.

PAGE 6/13 * RCVD AT 10/5/2004 4:36:24 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:703 905 2500 * DURATION (mm-ss):04-16

Amended claims 18 and 21 now depend from either claims 17 or 20 wherein proper antecedent basis exist for the plasmid vector comprising a nucleotide sequence encoding said malate:quinone oxidoreductase of *C. glutamicum* strain ATCC 13032. Amended claim 23 is now directed to the process according to claim 22, further comprising overexpression by increasing the copy number of one or more genes selected from the group consisting of a *dap*A gene encoding for dihydrodipicolinate synthase of *C. glutamicum* and a gene encoding for S-(2-aminoethyl)-cysteine resistance protein of *C. glutamicum*. The applicants submit the phrase "gene encoding an S-(2-aminoethyl)-cysteine resistance protein" clarifies the term at issue in claim 23 as suggested by the examiner.

In view of the foregoing amendment and remarks, the applicants respectfully submit that the rejection of claims 18, 21, and 23 pursuant to 35 U.S.C. §112, second paragraph, for allegedly being indefinite, has been overcome and should be withdrawn.

Rejection Pursuant to 35 U.S.C. §112, First Paragraph

Written Description

In paragraphs 8-11 of the official action, the examiner rejected claims 16, 19, 22, and 23 under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the written description requirement. Specifically, the examiner alleged that while overexpression of a gene by increasing the copy number is supported in the specification, other means of overexpression, such as mutating a promoter region of a recited gene or methods to lengthen the life of the corresponding mRNA, are not supported in the specification. Furthermore, the examiner asserted that the specification is silent with regard to the structural elements that are characteristics of any gene encoding an S-(2-aminoethyl)-cysteine resistance protein.

Amended claim 16 is directed to a fermentation process for the preparation of a desired L-amino acid selected from the group consisting of L-threonine and L-lysine wherein the following steps are carried out: (a) fermentation of an *Corynebacterium or Brevibacterium* strain in a fermentation broth for producing the desired L-amino acid, wherein a gene encoding malate:quinone oxidoreductase (*mqo*) of *Corynebacterium glutamicum* strain ATCC 13032 is **overexpressed by increasing the copy number** of said gene, (b) concentration of the fermentation broth to eliminate water and increase the concentration said L-amino acids in the broth and *Corynebacterium*, and (c) isolation of the L-amino acid from the fermentation broth and *Corynebacterium* of step (b).

PAGE 7/13 * RCVD AT 10/5/2004 4:36:24 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:703 905 2500 * DURATION (mm-ss):04-16

Amended claim 19 is directed to a fermentation process for the preparation of a desired L-amino acid selected from the group consisting of L-lysine, and L-methionine, wherein the following steps are carried out: (a) fermentation of an *C. glutamicum* strain in a fermentation broth for producing the desired L-amino acid, wherein a gene encoding malate:quinone oxidoreductase (*mqo*) of *C.glutamicum* strain ATCC 13032 is **overexpressed by increasing the copy number of said gene**.

Amended claim 22 is directed to a fermentation process for the preparation L-lysine, wherein the following steps are carried out (a) fermentation of an *Corynebacterium glutamicum* strain in a fermentation broth for producing L-lysine, wherein a gene encoding malate:quinone oxidoreductase (*mqo*) of *Corynebacterium glutamicum* strain ATCC 13032 is **overexpressed by increasing the copy number of said gene**, (b) concentration of the fermentation broth to eliminate water and increase the concentration said L-lysine in the broth and *Corynebacterium glutamicum* , and (c) isolation of the L-amino acid from the fermentation broth and *Corynebacterium glutamicum* of step (b). Amended claim 23 is directed to the process according to claim 22, further comprising **overexpression by increasing the copy number** of one or more genes selected from the group consisting of a *dapA* gene encoding dihydrodipicolinate synthase of *C. glutamicum* and **a gene encoding for S-(2-aminoethyl)-cysteine resistance protein of *C. glutamicum***.

Solely to expedite prosecution and without prejudice to the applicants' right seek broader claims in a continuing application, the applicants have indicated a particular mode of overexpression (*i.e.*, increasing the copy number of a gene) used to express the gene of interest. As acknowledged by the examiner, overexpression by increasing the copy number of a gene of interest is well known in the art. In addition, the applicants have indicated that the particular source of the gene encoding for S-(2-aminoethyl)-cysteine resistance protein is from *C. glutamicum*, which is fully supported throughout the specification, for example, on page 5, lines 29-32. In view of the foregoing amendment and remarks, the applicants submit the rejection of claims 16, 19, 22, and 23 under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the written description requirement, has been overcome and should be withdrawn.

Enablement-Alleged Conflicting Teachings of Copending U.S. Patent Appl. No. 10/118,325

In paragraphs 12-15 of the official action, the examiner has maintained her rejection of claims 16-23 under 35 U.S.C. §112, first paragraph, for allegedly lacking enablement with

PAGE 8/13 * RCVD AT 10/5/2004 4:36:24 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:703 905 2500 * DURATION (mm-ss):04-16

regard to the issue of allegedly conflicting teachings between this application and U.S. Patent Appl. No. 10/118,325 (Publication No. 20030044943). Specifically, the examiner asserted that the method of U.S. Patent Appl. No. 10/118,325 uses the same *mqo* gene (see Example 1 of 10/118,325) in the same process (Example 3 of 10/118,325), but for the fact that the host cell construct in 10/118,325 (DSM5715::pXK99Emobmqo) contains a fragment of the *C. glutamicum mqo* gene (incomplete gene) as opposed to a full length *mqo* gene taught in this application. The examiner alleged that absent experimental evidence explaining the contradicting results in the instant application and co-pending application 10/118,325, it is unclear as to how one of skill in the art can reasonably conclude that the claimed invention is enabled by the specification.

The applicants respectfully traverse the examiner's rejection under the enablement requirement. In determining whether a disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue," the following factors are considered: breadth of the claims, nature of the invention, state of prior art, level of one of ordinary skill, level of predictability in the art, amount of direction provided by inventor, existence of working examples, and quantity of experimentation needed to make or use the invention (See *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1999)). Specifically, a conclusion of non-enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation (*See In re Wright*, 999 F.2d 1557,1562 (Fed. Cir. 1993).

In this case, the examiner has used a post-filing dated reference to essentially allege that the claimed method of this application is not possible. Section 2164.05 (a) of the MPEP states that the examiner should not use post-filing date references to allege that the patent is non-enabling. The only exception to this general rule is the later dated reference must provide evidence that one of skill in the art would have known on or before the effective filing date of the patent application that the teachings of the application at issue are nonenabling (*See In re Hogan*, 559 F.2d 595, 605 (CCPA 1977). Only then would this be evidence for one of skill in the art to conclude that the disclosed invention was not possible at the time of filing. This is not the case here and accordingly, the examiner has erroneously applied this exception.

PAGE 9/13 * RCVD AT 10/5/2004 4:36:24 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:703 905 2500 * DURATION (mm-ss):04-16

Co-pending patent Appl. No. 10/118,325 teaches that attenuation of the *C. glutamicum mqo* gene in *C. glutamicum* results in the production of L-amino acids. This co-pending application, however, neither teaches nor suggests that an increase in L-amino acid production could not be achieved via overexpression of the *mqo* gene. Thus, one of skill in the art would not be able to conclude from the teachings of the co-pending application that the currently disclosed invention of this application was impossible. Rather, one of skill viewing the disclosure of the co-pending application would simply conclude attenuation may result in L-amino production as well.

The applicants submit that the examiner has improperly made a determination that the their application non-enabled even though (1) the applicants' teaching provides ample evidence that the overexpression of the full length *C. glutamicum mqo* gene increases L-amino acid production and (2) the applicants provided a declaration asserting these facts. As stated before on the record, Tables 1 and 2 of the specification clearly demonstrate overexpression of full length *mqo* gene increases L-amino acid production. Considering all the Wand factors, the specification is fully enabled for the claimed methods. In contrast to any merit, it seems as if the examiner's enablement rejection is based solely on her personal opinion, which basis **is forbidden by the Patent Office**. See MPEP §2164.05.

In view of the foregoing remarks, the applicants respectfully submit that this portion of the rejection of claims 16-23 under 35 U.S.C. §112, first paragraph, for lacking a proper enabling disclosure, has been overcome and should be withdrawn.

Other Alleged Enablement Issues

In paragraph 16-19 of the official action, the examiner further rejected claims 16-23 under 35 U.S.C. §112, first paragraph, for allegedly lacking enablement. Specifically, the examiner alleged that while the specification was enabling for a method of producing L-lysine and L-threonine in *Corynebacterium* and *Brevibacterium* wherein the *mqo* gene is overexpressed by increasing the copy number of said gene, the specification is not enabled for method as described above for the production of L-aspartic acid, L-asparagine, L-homoserine, L-isoleucine, or L-methionine by overexpressing the *mqo* gene by using altered promoters or extending the life of corresponding mRNAs. The examiner also alleged that the claimed method is not enabled for overexpressing any gene encoding an S-(2-aminoethyl)-cysteine resistance protein.

PAGE 10/13 * RCVD AT 10/5/2004 4:36:24 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:703 905 2500 * DURATION (mm-ss):04-16

The applicants respectfully submit that the specification provides ample examples of the claimed methods described above for production of L-aspartic acid, L-asparagine, L-homoserine, L-isoleucine, or L-methionine. Section 2164.02 of the MPEP states that although the lack of a working example may be a factor to consider in determining an enabling disclosure, the applicants need not describe all actual embodiments if the invention is disclosed in such a manner that one skill in the art will be able to practice it without undue amount of experimentation. In this case, the specification has provided two working examples of measuring for L-lysine or L-threonine in recombinant *C. glutamicum* or Brevibacterium strains which are overexpressing the *C. glutamicum mqo* gene. In both examples, the concentration of L-lysine and L-threonine were determined using an amino acid analyzer from Eppendorf-BioTronik. One of skill in the art would be able to practice the claimed methods as taught by the specification to produce and measure L-aspartic acid, L-asparagine, L-homoserine, L-isoleucine, or L-methionine in a fermentation broth. The examiner's argument that undue experimentation is required to place a plasmid which overexpresses the *mqo* gene and measure for an increase in production of either L-aspartic acid, L-asparagine, L-homoserine, L-isoleucine, or L-methionine **lacks merit** considering the fermentative arts. One of skill in the art, by routine methods, transforms a plasmid harboring the *C. glutamicum mqo* gene, such as pRM17 into *C. glutamicum*. Next, one of skill ferments the bacterium under the described broth conditions described on page 8 of the specification. Finally, one of skill measures for the L-amino acid of interest using an amino acid analyzer. None of these steps involve undue experimentation. In contrast to the examiner's allegations, the specification provides sufficient evidence that these amino acids can be prepared and measured by the claimed methods.

Nevertheless, solely to expedite prosecution and without prejudice to pursuing broader claims in a continuing application, the applicants have amended claim 16-23 as discussed above. Specifically, the amended claims 16-22 are now directed to specific fermentation processes of the production L-lysine and L-threonine in *Corynebacterium* and *Brevibacterium* wherein the *mqo* gene is overexpressed by increasing the copy number of said gene. Amended 23 is now directed to the claimed methods of claim 22 and in addition, increasing the copy number of the *C. glutamicum* gene encoding for S-(2-aminoethyl)-cysteine resistance. The applicant respectfully submit the source of the gene encoding for S-(2-aminoethyl)-cysteine resistance (*i.e., C. glutamicum*) is fully described and enabled throughout the specification. In view of the foregoing amendment and remarks, the

applicants respectfully submit the rejection of claims 16-23 under 35 U.S.C. §112, first paragraph, for lack of enablement, has been overcome and should be withdrawn.

Rejection Pursuant to the Judicially Created Doctrine of Obviousness-Type Double Patenting

In paragraph 20-27 of the official action, the examiner provisionally rejected claims 16, 17, 19, 20, 22, and 23 under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claim 10 of co-pending U.S. Patent Appl. No. 10/178,219, claim 14 of co-pending U.S. Patent Appl. No. 10/375,355, and claim 18 of co-pending U.S. Patent Appl. No. 09/938,540.

The applicants submit that this rejection is improper. In view of the fact that the aforementioned applications were filed after the present application, a two-way obviousness test is required (application of the *Graham* obviousness analysis twice). See MPEP § 804. The examiner has not provided the required analysis, thus the rejection is improper.

PAGE 12/13 * RCVD AT 10/5/2004 4:36:24 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:703 905 2500 * DURATION (mm-ss):04-16

CONCLUSION

In view of the foregoing, the claims are now believed to be in form for allowance, and such action such action is hereby solicited. If any point remains in issue which the examiner feels may be best resolved through a personal or telephone interview, please contact the undersigned at the telephone number listed below.

Respectfully submitted,

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PAGE 13/13 * RCVD AT 10/5/2004 4:36:24 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:703 905 2500 * DURATION (mm-ss):04-16